

Claims

What is claimed is:

1. A method for enhancing the delivery of a drug to a tumor in a mammal, comprising administering to a mammal a cell adhesion modulating agent and a drug, wherein said modulating agent comprises the sequence LYHY (SEQ ID NO:1), and wherein said modulating agent inhibits occludin-mediated cell adhesion.

2. A method for enhancing the delivery of a drug to a tumor in a mammal, comprising administering to a mammal a cell adhesion modulating agent and a drug, wherein said modulating agent comprises an antibody or fragment thereof that specifically binds to an occludin cell adhesion recognition sequence, and wherein said modulating agent inhibits occludin-mediated cell adhesion.

3. A method according to claim 1 or claim 2, wherein the tumor is selected from the group consisting of bladder tumors, ovarian tumors and melanomas.

4. A method according to claim 1 or claim 2, wherein said composition is administered to said tumor.

5. A method according to claim 1 or claim 2, wherein said composition is administered systemically.

6. A method according to claim 1, wherein said modulating agent comprises a sequence selected from the group consisting of QYLYHYCVVD (SEQ ID NO:2), YLYHYCVVD (SEQ ID NO:12), LYHYCVVD (SEQ ID NO:13), QYLYHYC (SEQ ID NO:14), YLYHYC (SEQ ID NO:15), LYHYC (SEQ ID NO:16), QYLYHY (SEQ ID NO:17), YLYHY (SEQ ID NO:18), CLYHYC (SEQ ID NO:3), CYLYHYC (SEQ ID NO:40), CQYLYHYC (SEQ ID NO:41), KQYLYHYD (SEQ ID NO:42), YLYHY (SEQ ID NO:43), QYLYHY (SEQ ID NO:44), KLYHYD (SEQ ID NO:45)

and derivatives of the foregoing sequences having one or more C-terminal, N-terminal and/or side chain modifications.

7. A method according to claim 1 or claim 2, wherein said modulating agent is linked to a targeting agent.

8. A method according to claim 1 or claim 2, wherein said modulating agent is linked to said drug.

9. A method according to claim 1 or claim 2, wherein said modulating agent further comprises one or more of:

(a) a cell adhesion recognition sequence bound by an adhesion molecule other than an occludin, wherein said cell adhesion recognition sequence is separated from any LYHY (SEQ ID NO:1) sequence(s) by a linker; and/or

(b) an antibody or antigen-binding fragment thereof that binds to a cell adhesion recognition sequence bound by an adhesion molecule other than an occludin.

10. A method according to claim 9, wherein said cell adhesion recognition sequence comprises one or more sequences selected from the group consisting of HAV, NQK, NRN, NKD, EKD, ERD, RGD, DDK, EEY, EAQ, IYSY (SEQ ID NO:49), TSSY (SEQ ID NO:50), VTAF (SEQ ID NO:51) and VSAF (SEQ ID NO:52).

11. A method according to claim 9, wherein said antibody or antigen-binding fragment thereof binds to a cell adhesion recognition sequence comprising a sequence selected from the group consisting of HAV, NQK, NRN, NKD, EKD, ERD, RGD, DDK, EEY, EAQ, IYSY (SEQ ID NO:49), TSSY (SEQ ID NO:50), VTAF (SEQ ID NO:51) and VSAF (SEQ ID NO:52).

12. A method according to claim 1 or claim 2, wherein said modulating agent and said drug are present within a pharmaceutical composition comprising a pharmaceutically acceptable carrier.

13. A method according to claim 12, wherein said pharmaceutical composition further comprises a modulator of cell adhesion comprising one or more of:

- (a) a cell adhesion recognition sequence bound by an adhesion molecule other than an occludin; and/or
- (b) an antibody or antigen-binding fragment thereof that binds to a cell adhesion recognition sequence bound by an adhesion molecule other than an occludin.

14. A method according to claim 13, wherein said cell adhesion recognition sequence comprises one or more sequences selected from the group consisting of HAV, NQK, NRN, NKD, EKD, ERD, RGD, DDK, EEY, EAQ, IYSY (SEQ ID NO:49), TSSY (SEQ ID NO:50), VTAF (SEQ ID NO:51) and VSAF (SEQ ID NO:52).

15. A method according to claim 13, wherein said antibody or antigen-binding fragment thereof binds to a cell adhesion recognition sequence comprising a sequence selected from the group consisting of HAV, NQK, NRN, NKD, EKD, ERD, RGD, DDK, EEY, EAQ, IYSY (SEQ ID NO:49), TSSY (SEQ ID NO:50), VTAF (SEQ ID NO:51) and VSAF (SEQ ID NO:52).

16. A method for treating cancer in a mammal, comprising administering to a mammal a cell adhesion modulating agent, wherein said modulating agent comprises the sequence LYHY (SEQ ID NO:1), and wherein said modulating agent inhibits occludin-mediated cell adhesion.

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17. A method for treating cancer in a mammal, comprising administering to a mammal a cell adhesion modulating agent, wherein said modulating agent comprises an antibody or fragment thereof that specifically binds to an occludin cell adhesion recognition sequence, and wherein said modulating agent inhibits occludin-mediated cell adhesion.

18. A method according to claim 16 or claim 17, wherein said cancer is selected from the group consisting of carcinomas, leukemia and melanomas.

19. A method according to claim 16, wherein said modulating agent comprises a sequence selected from the group consisting of QYLYHYCVVD (SEQ ID NO:2), YLYHYCVVD (SEQ ID NO:12), LYHYCVVD (SEQ ID NO:13), QYLYHYC (SEQ ID NO:14), YLYHYC (SEQ ID NO:15), LYHYC (SEQ ID NO:16), QYLYHY (SEQ ID NO:17), YLYHY (SEQ ID NO:18), CLYHYC (SEQ ID NO:3), CYLYHYC (SEQ ID NO:40), CQYLYHYC (SEQ ID NO:41), KQYLYHYD (SEQ ID NO:42), YLYHY (SEQ ID NO:43), QYLYHY (SEQ ID NO:44), KLYHYD (SEQ ID NO:45) and derivatives of the foregoing sequences having one or more C-terminal, N-terminal and/or side chain modifications.

20. A method according to claim 16 or claim 17, wherein said modulating agent is linked to a targeting agent.

21. A method according to claim 16 or claim 17, wherein said modulating agent further comprises one or more of:

(a) a cell adhesion recognition sequence bound by an adhesion molecule other than an occludin, wherein said cell adhesion recognition sequence is separated from any LYHY (SEQ ID NO:1) sequence(s) by a linker; and/or

(b) an antibody or antigen-binding fragment thereof that binds to a cell adhesion recognition sequence bound by an adhesion molecule other than an occludin.

22. A method according to claim 21, wherein said cell adhesion recognition sequence comprises a sequence selected from the group consisting of HAV, NQK, NRN, NKD, EKD, ERD, RGD, DDK, EEY, EAQ, IYSY (SEQ ID NO:49), TSSY (SEQ ID NO:50), VTAF (SEQ ID NO:51) and VSAF (SEQ ID NO:52).

23. A method according to claim 16 or claim 17, wherein said modulating agent is present within a pharmaceutical composition comprising a pharmaceutically acceptable carrier.

24. A method according to claim 16 or claim 17, wherein said pharmaceutical composition further comprises a modulator of cell adhesion comprising one or more of:

- (a) a cell adhesion recognition sequence bound by an adhesion molecule other than an occludin; and/or
- (b) an antibody or antigen-binding fragment thereof that binds to a cell adhesion recognition sequence bound by an adhesion molecule other than an occludin.

25. A method according to claim 24, wherein said cell adhesion recognition sequence comprises a sequence selected from the group consisting of HAV, NQK, NRN, NKD, EKD, ERD, RGD, DDK, EEY, EAQ, IYSY (SEQ ID NO:49), TSSY (SEQ ID NO:50), VTAF (SEQ ID NO:51) and VSAF (SEQ ID NO:52).

26. A method for enhancing immune cell infiltration into a tumor in a mammal, comprising administering to a mammal a cell adhesion modulating agent and a drug, wherein said modulating agent comprises the sequence LYHY (SEQ ID NO:1), and wherein said modulating agent inhibits occludin-mediated cell adhesion.

27. A method for enhancing immune cell infiltration into a tumor in a mammal, comprising administering to a mammal a cell adhesion modulating agent and a drug, wherein said modulating agent comprises an antibody or fragment thereof that specifically binds to an occludin cell adhesion recognition sequence, and wherein said modulating agent inhibits occludin-mediated cell adhesion.

28. A method according to claim 26 or claim 27, wherein the tumor is selected from the group consisting of bladder tumors, ovarian tumors and melanomas.

29. A method according to claim 26 or claim 27, wherein said composition is administered to said tumor.

30. A method according to claim 26 or claim 27, wherein said composition is administered systemically.

31. A method according to claim 26, wherein said modulating agent comprises a sequence selected from the group consisting of QYLYHYCVVD (SEQ ID NO:2), YLYHYCVVD (SEQ ID NO:12), LYHYCVVD (SEQ ID NO:13), QYLYHYC (SEQ ID NO:14), YLYHYC (SEQ ID NO:15), LYHYC (SEQ ID NO:16), QYLYHY (SEQ ID NO:17), YLYHY (SEQ ID NO:18), CLYHYC (SEQ ID NO:3), CYLYHYC (SEQ ID NO:40), COYLYHYC (SEQ ID NO:41), KQYLYHYD (SEQ ID NO:42), YLYHY (SEQ ID NO:43), QYLYHY (SEQ ID NO:44), KLYHYD (SEQ ID NO:45) and derivatives of the foregoing sequences having one or more C-terminal, N-terminal and/or side chain modifications.

32. A method according to claim 26 or claim 27, wherein said modulating agent is linked to a targeting agent.

²³33. A method according to claim ²⁶26 or claim ²⁷27, wherein said modulating agent and said drug are present within a pharmaceutical composition comprising a pharmaceutically acceptable carrier.